



## Complete Summary

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### GUIDELINE TITLE

Diagnosis and treatment of osteoporosis.

### BIBLIOGRAPHIC SOURCE(S)

Institute for Clinical Systems Improvement (ICSI). Diagnosis and treatment of osteoporosis. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2004 Jul. 66 p. [175 references]

## COMPLETE SUMMARY CONTENT

SCOPE  
METHODOLOGY - including Rating Scheme and Cost Analysis  
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CONTRAINDICATIONS  
QUALIFYING STATEMENTS  
IMPLEMENTATION OF THE GUIDELINE  
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT  
CATEGORIES  
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## SCOPE

### DISEASE/CONDITION(S)

Osteoporosis

### GUIDELINE CATEGORY

Diagnosis  
Evaluation  
Prevention  
Risk Assessment  
Treatment

### CLINICAL SPECIALTY

Endocrinology  
Family Practice  
Geriatrics  
Internal Medicine

Preventive Medicine  
Rheumatology

## INTENDED USERS

Advanced Practice Nurses  
Allied Health Personnel  
Health Care Providers  
Health Plans  
Hospitals  
Managed Care Organizations  
Nurses  
Physician Assistants  
Physicians

## GUIDELINE OBJECTIVE(S)

- To improve diagnostic and therapeutic follow-up of adults presenting with a history of low impact fracture
- To increase the evaluation for osteoporosis risk factors in all adults presenting for a preventive visit
- To increase follow-up testing of patients on long term hormone replacement therapy (HRT)

## TARGET POPULATION

- Men and women at risk for osteoporosis
- Men and women with suspected or confirmed osteoporosis

## INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis; Risk Assessment/Prognosis; Evaluation

1. Assessment for and discussion of risk factors for osteoporosis
2. Serial height measurements with a stadiometer
3. Assessment of posture
4. Radiographs of the thoracic and lumbar spine as indicated
5. Measurement of bone mineral density (BMD) as indicated
6. Laboratory evaluation of patients with osteoporosis to assess for secondary causes of osteoporosis (tests vary depending on patient features)

Prevention and/or Treatment of Osteoporosis

1. Lifestyle counseling regarding measures to prevent fractures (exercise, smoking cessation, alcohol restriction, dietary counseling, weight, environmental modification to prevent falls, measures to reduce the impact of falls [such as soft hip protector pads])
2. Vitamin D and calcium supplementation
3. Pharmacologic agents
  - Bisphosphonates (alendronate [Fosamax®] and risedronate [Actonel®]) (treatment and prevention)

- Selective estrogen receptor modulator (SERM) (Raloxifene [Evista®]) (treatment and prevention)
  - Calcitonin (Calcitonin-salmon [Miacalcin® injection and nasal spray, Calcimar® injection, Salmonine® injection, Osteocalcin® injection]) (treatment)
  - Estrogens (prevention)
4. Physical therapy
  5. Alternative and complementary agents (phytoestrogens, synthetic isoflavones such as ipriflavone, natural progesterone cream, magnesium, vitamin K, and eicosapentaenoic acid)
  6. Follow-up bone mineral density testing (with dual x-ray absorptiometry [DXA] at a central site [lumbar spine and/or total hip]) after pharmacologic intervention to assess changes in bone mineral density.

#### Note

- Guideline developers considered, but did not recommend follow-up bone density testing at peripheral sites (forearm DXA, calcaneal DXA, or calcaneal ultrasound)
- Guideline developers listed and commented on, but did not recommend, the following non-FDA-approved treatments for osteoporosis: (bisphosphonates: etidronate [Didronel®], pamidronate [Aredia®], and zoledronic acid [Zometa®]; calcitriol [Rocaltrol®]; ergocalciferol [Calciferol®]; nandrolone decanoate; parathyroid hormone [PTH]; sodium fluoride; tamoxifen [Nolvadex®]; testosterone; tibolone)

#### MAJOR OUTCOMES CONSIDERED

- Fracture risk (absolute risk, relative risk, and incidence)
- Predictive value of bone mineral density measurements
- Effects of prevention/treatment interventions on bone density, bone loss, bone health, and fracture risk

### METHODOLOGY

#### METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

#### DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

No additional description of literature search strategies is available.

#### NUMBER OF SOURCE DOCUMENTS

Not stated

#### METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

## Weighting According to a Rating Scheme (Scheme Given)

### RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Key conclusions (as determined by the work group) are supported by a conclusion grading worksheet that summarizes the important studies pertaining to the conclusion. Individual studies are classed according to the system presented below and are designated as positive, negative, or neutral to reflect the study quality.

#### Conclusion Grades:

**Grade I:** The evidence consists of results from studies of strong design for answering the question addressed. The results are both clinically important and consistent with minor exceptions at most. The results are free of any significant doubts about generalizability, bias, and flaws in research design. Studies with negative results have sufficiently large samples to have adequate statistical power.

**Grade II:** The evidence consists of results from studies of strong design for answering the question addressed, but there is some uncertainty attached to the conclusion because of inconsistencies among the results from the studies or because of minor doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from weaker designs for the question addressed, but the results have been confirmed in separate studies and are consistent with minor exceptions at most.

**Grade III:** The evidence consists of results from studies of strong design for answering the question addressed, but there is substantial uncertainty attached to the conclusion because of inconsistencies among the results of different studies or because of serious doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from a limited number of studies of weak design for answering the question addressed.

**Grade Not Assignable:** There is no evidence available that directly supports or refutes the conclusion.

#### Study Quality Designations:

The quality of the primary research reports and systematic reviews are designated in the following ways on the conclusion grading worksheets:

**Positive:** indicates that the report or review has clearly addressed issues of inclusion/exclusion, bias, generalizability, and data collection and analysis.

**Negative:** indicates that these issues (inclusion/exclusion, bias, generalizability, and data collection and analysis) have not been adequately addressed.

**Neutral:** indicates that the report or review is neither exceptionally strong nor exceptionally weak.

Not Applicable: indicates that the report is not a primary reference or a systematic review and therefore the quality has not been assessed.

#### Classes of Research Reports:

##### A. Primary Reports of New Data Collection:

###### Class A:

- Randomized, controlled trial

###### Class B:

- Cohort study

###### Class C:

- Non-randomized trial with concurrent or historical controls
- Case-control study
- Study of sensitivity and specificity of a diagnostic test
- Population-based descriptive study

###### Class D:

- Cross-sectional study
- Case series
- Case report

##### B. Reports that Synthesize or Reflect upon Collections of Primary Reports:

###### Class M:

- Meta-analysis
- Systematic review
- Decision analysis
- Cost-effectiveness analysis

###### Class R:

- Consensus statement
- Consensus report
- Narrative review

###### Class X:

- Medical opinion

#### METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses  
Systematic Review with Evidence Tables

## DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

## METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

## RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

## COST ANALYSIS

The guideline developers reviewed published cost analysis.

## METHOD OF GUIDELINE VALIDATION

Clinical Validation-Pilot Testing  
Internal Peer Review

## DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Institute Partners: System-Wide Review

The guideline draft, discussion, and measurement specification documents undergo thorough review. Written comments are solicited from clinical, measurement, and management experts from within the member medical groups during an eight-week period of "Critical Review."

Each of the Institute's participating medical groups determines its own process for distributing the guideline and obtaining feedback. Clinicians are asked to suggest modifications based on their understanding of the clinical literature coupled with their clinical expertise. Representatives from all departments involved in implementation and measurement review the guideline to determine its operational impact. Measurement specifications for selected measures are developed by the Institute for Clinical Systems Improvement (ICSI) in collaboration with participating medical groups following general implementation of the guideline. The specifications suggest approaches to operationalizing the measure.

Guideline Work Group: Second Draft

Following the completion of the "Critical Review" period, the guideline work group meets 1 to 2 times to review the input received. The original guideline is revised as necessary, and a written response is prepared to address each of the suggestions received from medical groups. Two members of the Committee on Evidence-Based Practice carefully review the Critical Review input, the work group responses, and the revised draft of the guideline. They report to the entire committee their assessment of two questions: (1) Have the concerns of the medical groups been adequately addressed? (2) Are the medical groups willing

and able to implement the guideline? The committee then either approves the guideline for pilot testing as submitted or negotiates changes with the work group representative present at the meeting.

#### Pilot Test

Medical groups introduce the guideline at pilot sites, providing training to the clinical staff and incorporating it into the organization's scheduling, computer and other practice systems. Evaluation and assessment occur throughout the pilot test phase, which usually lasts for three months. Comments and suggestions are solicited in the same manner as used during the "Critical Review" phase.

The guideline work group meets to review the pilot sites' experiences and makes the necessary revisions to the guideline, and the Committee on Evidence-Based Practice reviews the revised guideline and approves it for implementation.

## RECOMMENDATIONS

### MAJOR RECOMMENDATIONS

The recommendations for the diagnosis and treatment of osteoporosis are presented in the form of an algorithm with 16 components, accompanied by detailed annotations. An algorithm is provided for [Bone Health](#); clinical highlights and selected annotations (numbered to correspond with the algorithm) follow.

Class of evidence (A-D, M, R, X) and conclusion grade (I-III, Not Assignable) definitions are repeated at the end of the "Major Recommendations" field.

#### Clinical Highlights

1. Discuss risk factors for osteoporosis and primary prevention with all patients presenting for preventive health visits. (Annotations #4, 5)
2. Patients with a high pretest probability of low bone mineral density (BMD) and future fracture should have bone density testing to further define their fracture risk. (Annotation #8)
3. Address pharmacologic options for prevention and treatment of osteoporosis with appropriate patients at risk for or who currently have signs and symptoms of osteoporosis. (Annotation #15)

#### Diagnosis and Treatment of Osteoporosis Algorithm Annotations

##### 1. All Patients Presenting for a Preventive Visit

Osteoporosis is the consequence of continued bone loss throughout adulthood. The guideline developers recommend maintaining peak bone mass for all patients. To achieve this, patients should have risks for osteoporosis reviewed when they present to their provider offices. In addition to reviewing historical risk factors (discussed in Annotation #4, "Discuss Risk Factors for Osteoporosis and Osteoporotic Fracture"), it is important to record accurate serial height measurements with a stadiometer and observe posture for kyphosis. Patients with significant acquired kyphosis and/or a height loss of

one inch should have thoracic and lumbar spine radiographs and bone density testing.

Evidence supporting this recommendation is of class: R

## 2. Patient With a Low-Impact Fracture

Discuss osteoporosis risk with any adult who has a history of a low-trauma fracture that may be related to osteoporosis. For the purpose of this guideline, a low-impact fracture will be defined as a fracture occurring spontaneously or from a fall at a height no greater than the patient's standing height, including fragility fractures occurring from activities such as a cough, sneeze, or abrupt movement (e.g., opening a window), and patients who have vertebral compression fracture documentation on radiographs regardless of their degree of symptoms. Many adults do not realize that having one fracture in their adult lifetime indicates an increased risk of future fractures and may be an indication for bone density testing. This historical risk factor provides information that may be additive to bone mineral density information. There are three possible hypotheses to explain this increased risk. First, risk factors for the development of one fracture are still operative to increase susceptibility to a second and subsequent event. Second, the occurrence of a fracture, particularly in the limbs, is followed by bone loss, not completely reversible, which could lead to an increased risk of subsequent fracture. Finally, there may be mechanical influences caused by having had one fracture, and it may be these mechanical effects that increase this subsequent risk.

### Post-Fracture Recommendations

- Consider all adults with a history of vertebral fracture, hip fracture, or distal forearm fracture at higher than average risk for a future fracture.
- Review lifestyle risk factors for osteoporosis. Discuss adequacy of total calcium and vitamin D intake. Address home safety and fall prevention.
- Consider bone density testing in fracture patients willing to accept treatment.
- Consider all men\* and postmenopausal women with low impact fracture as candidates for osteoporosis treatment.
- Adults over age 70 with prior fracture are candidates for osteoporosis therapy even without bone density testing.

\*Although the best data available is on postmenopausal women, there may be a similar risk in men, and the guideline developers are including men in this guideline recommendation. [Melton LJ III, Atkinson EJ, O'Connor MK, et al. Bone density and fracture risk in men. J Bone Mineral Res 13: 1915-23, 1998.]

Evidence supporting this recommendation is of classes: A, B, C, D, M, R

### 3. Patient Started On or Continuing Chronic Glucocorticoid Steroid Use or Transplant Recipient

#### Glucocorticoid Steroid Use

Osteoporosis prevention and treatment measures and bone mineral density testing should be considered for anyone who is started on or has been on exogenous systemic glucocorticoid therapy (at a dose of more than 7.5 mg of prednisone per day or equivalent per day for 3 or more months). While it is never too late in the course of glucocorticoid therapy to prevent or treat osteoporosis, it is preferable to start preventive measures against bone loss at the time glucocorticoids are commenced because the greatest amount of bone is lost during the first several months of glucocorticoid use. Osteoporosis prevention measures should also be considered for those who have been or can be expected to be on daily use high-dose inhaled glucocorticoids for several years.

#### Organ Transplantation

Solid organ transplantation of all types and allogeneic bone marrow transplantation are associated with rapid bone loss after transplantation. In addition, many patients develop significant bone loss before transplantation.

Evidence supporting this recommendation is of classes: , B, D

### 4. Discuss Risk Factors for Osteoporosis and Osteoporotic Fracture

The following are risk factors for osteoporosis and osteoporotic fracture:

- Female
- Advanced age (greater than age 65)
- Body habitus (weight less than 127 pounds; or body mass index [BMI]  $\leq 20$ )
- Caucasian or Asian race
- Family history of osteoporosis
- Hypogonadism (estrogen or testosterone deficiency)
- Sedentary lifestyle
- Smoking (one or more packs per day)
- Excessive alcohol intake (more than two drinks per day)
- Diet deficient in calcium or vitamin D without adequate supplementation
- Increased likelihood of falling

For a list of secondary causes of osteoporosis, please see Annotation Appendix A, "Secondary Causes of Osteoporosis" in the original guideline document.

Evidence supporting this recommendation is of classes: A, B, C, D, M, R

### 5. Discuss Primary Prevention of Fractures

## Body Habitus

Patients should be counseled that a body mass index of less than 20, or weight less than 127 pounds increases their risk of osteoporotic fractures.

Evidence supporting this recommendation is of class: B

## Gonadal Hormonal Status

Patients who are deficient in estrogen or testosterone are at increased risk for fracture and should be offered replacement therapy. For further information, please see Discussion #14, "Consider Secondary Causes and Further Diagnostic Testing" as well as Discussion #15, "Address Options for Prevention or Treatment of Osteoporosis" in the original guideline document.

## Exercise

Exercise is well known for its many benefits both short-term and long-term. Weight bearing and muscle strengthening exercises have been shown to be an integral part of osteoporosis prevention as well as a part of the treatment process.

Evidence supporting this recommendation is of classes: D, R

## Smoking Cessation

Smoking cessation counseling should be done at every visit. Discussion can include helpful strategies such as nicotine replacement therapy with patches, gum, etc. Bupropion and available smoking cessation classes may also be discussed. For more information on smoking cessation, please refer to the National Guideline Clearinghouse (NGC) summary of the Institute for Clinical Systems Improvement (ICSI) guideline, [Tobacco Use Prevention and Cessation for Adults and Mature Adolescents](#).

## Alcohol Restriction

Limit alcohol use to no more than two drinks per day. One drink equals 12 ounces of beer, 5 ounces of wine, or 1.5 ounces of 80-proof distilled spirits. This limit will help to protect bone health and reduce the risk of falls.

Evidence supporting this recommendation is of classes: A, D, R

## Calcium

Adequate calcium intakes from food sources and supplements promote bone health. Calcium also supports estrogen's positive effect on bone health. When food sources do not provide enough calcium, supplements can be used to meet this goal. Bioavailability of calcium in food sources and supplements is a factor in achieving daily calcium recommendations. Calcium supplement labels should indicate lead testing.

Daily elemental calcium recommendations for healthy individuals include:

National Academy of Sciences, Institute of Medicine (1997)

- 9-18 years: 1,300 mg.
- 19-50 years: 1,000 mg.
- Over 50 years: 1,200 mg.
- Maximum limit: 2,500 mg.

However, for people with established osteoporosis, glucocorticoid use, pregnant or nursing women, or persons over the age of 65, it may be more appropriate to recommend 1,500 mg.

Calcium slows age-related bone loss. [Conclusion Grade II, See Conclusion Grading Worksheet - Appendix A of the original guideline document, - Annotations #4 & 5 (Calcium)]

Calcium may reduce osteoporosis fracture risk. [Conclusion Grade III, See Conclusion Grading Worksheet - Appendix A of the original guideline document, - Annotations # 4 & 5 (Calcium)]

## Vitamin D

Adequate vitamin D intake supports calcium absorption and bone metabolism. Since sunlight exposure cannot be assumed to produce needed vitamin D, dietary sources are essential. Since many adults in northern climates are deficient in vitamin D, supplements are often needed to meet daily requirements. The following guidelines assume no vitamin D is synthesized from sunlight exposure:

Institute of Medicine (1997)

- 19-50 years: 200 IU/day
- 51-70 years: 400 IU/day
- over 70 years: 600 IU/day
- Maximum limit: 2,000 IU/day

## Prevention of Falls

Preventing falls reduces fractures and fracture risk. Modifying environmental personal risk and medication-related factors can be effective in reducing falls. Home visits may help with this. Hip protector pads for frail, elderly adults have been shown to reduce hip fractures in some studies.

## 6. Low Pre-Test Probability of Low BMD and Future Fracture

The following individuals are at low risk of low bone density and future fracture

1. Premenopausal women who have not had a fracture with minor trauma, are not on chronic glucocorticoid therapy, do not have

- secondary amenorrhea, and do not have a chronic disease associated with bone loss
- 2. Eugonadal men who have not had a fracture with minor trauma, are not on glucocorticoid therapy, and do not have another chronic disease associated with bone loss
- 3. Postmenopausal women under age 65 who have been on hormone replacement therapy since menopause and who do not have any significant additional risk factors.

Evidence supporting this recommendation is of classes: C, D, M, R

#### 7. Address/Reinforce Options for Prevention of Osteoporosis

Osteoporosis is the consequence of continued bone loss throughout adulthood. Because of this, providers are encouraged to periodically review historical risk factors (see Annotation #4, "Discuss Risk Factors for Osteoporosis and Osteoporotic Fracture") and primary prevention strategies (see Annotation #5, "Discuss Primary Prevention of Fractures") with their patients. Preventive health maintenance exams provide an excellent opportunity for this review.

#### 8. High Pre-Test Probability of Low BMD and Future Fracture

The following individuals are at sufficiently high risk for low bone mass and future fracture that a bone mineral density test is justified to further define that risk. This assumes that the individual being tested is willing to consider pharmacologic treatment for low bone mass documented on a bone density test. The first three of these indicate individuals at particularly high risk of bone loss and future fracture.

- 1. Prior fracture with minor trauma (fall from standing height or less)
- 2. Those who have been, or are anticipated to be on glucocorticoid therapy, for 3 or more months at a dose equivalent to or greater than 7.5 mg prednisone per day
- 3. Radiographic osteopenia or vertebral deformity consistent with fracture
- 4. All women greater than 65 years of age
- 5. Postmenopausal women less than age 65 with one of the following additional risk factors
  - a. Body weight less than 127 lbs or body mass index  $\leq 20$
  - b. History of nontraumatic fracture after age 45 in a first-degree relative
  - c. Current smoker (one pack or more per day)
  - d. Not using hormone replacement therapy
  - e. Surgical menopause, or natural menopause before age 40
  - f. On hormone replacement therapy greater than 10 to 15 years
- 6. Chronic diseases known to be associated with bone loss (see Annotation Appendix A, "Secondary Causes of Osteoporosis" in the original guideline document)
- 7. Premenopausal women with amenorrhea greater than 1 year
- 8. Men with hypogonadism more than 5 years
- 9. Prolonged severe loss of mobility (unable to ambulate outside of one's dwelling without a wheelchair for greater than one year)

## 10. Transplant recipient

Evidence supporting this recommendation is of classes: C, D, M, R

### 9. Recommend Bone Density Assessment

Measurements of BMD can predict fracture risk and allow for the identification of people who are at increased risk of fracture. Reviews of prospective cohort studies and case control studies have documented a direct relationship between decreasing BMD and increasing bone fracture risk. Additionally, there is strong evidence that increases in BMD with therapy for osteoporosis lead to substantial reductions in fracture incidence. Therefore, densitometry offers an objective measurement of a patient's response to treatment over time.

Current practice is to describe an individual's bone mineral density as compared to a reference normal population. In this sense, a T-score is the number of standard deviations above or below the mean for a young adult healthy population. A T-score is calculated from the following equation:

$$\frac{[(\text{measured BMD} - \text{young adult population mean BMD}) / \text{young adult population SD}]}$$

A Z-score is the number of standard deviations above or below the mean for an age- and sex-matched healthy population. A Z-score is calculated from the following equation:

$$\frac{[(\text{measured BMD} - \text{age-matched population mean BMD}) / \text{age-matched population SD}]}$$

Normal, osteopenia, and osteoporosis are defined by the T-score, according to the World Health Organization (WHO). Although the following classifications were originally drafted for Caucasian postmenopausal women, some controversy exists as to whether the same diagnostic criteria can be applied to other groups.

- Normal: A T-score greater than or equal to -1
- Osteopenia: A T-score between -1 and -2.5
- Osteoporosis: A T-score less than or equal to -2.5
- The term "severe osteoporosis" is reserved for patients with both a fragility fracture(s) and a T-score less than or equal to -2.5.

For patients who decline bone density testing, reinforce osteoporosis prevention, consider gonadal hormone replacement therapy, and follow-up discussion of osteoporosis at future preventive visits.

Evidence supporting this recommendation is of classes: C, M, R

### 10. Post-Test Probability

The result of the bone mineral density test is the best single predictor of future fracture risk.

Evidence supporting this recommendation is of classes: B, C

#### 11. Low Risk of Future Fracture

Low fracture risk is clinically defined by a bone mineral density T-score above -1.0 (normal bone density by the WHO definition).

Evidence supporting this recommendation is of classes: B, R

#### 12. Moderate Risk of Future Fracture

Moderate fracture risk is clinically defined by a bone mineral density T-score below -1.0 and above -2.5 (osteopenia by the WHO definition).

Evidence supporting this recommendation is of classes: B, R

#### 13. High Risk of Future Fracture

High fracture risk is clinically defined by a bone mineral density T-score below -2.5 (osteoporosis density by the WHO definition).

Evidence supporting this recommendation is of classes: B, R

#### 14. Consider Secondary Causes and Further Diagnostic Testing

A minimum screening laboratory profile should be considered in all patients with osteoporosis. Expert opinion in the literature varies regarding the degree of laboratory investigation indicated in the osteoporotic patient with a bone density at the age-matched value, but it is agreed that a more extensive evaluation is indicated to look for a potentially reversible cause of lower than expected bone density (Z-score less than or equal to -1). See discussion section of the original guideline document for additional information on lab testing.

At this time there is no consensus about the routine use of serum and/or urine markers of bone turnover in the evaluation of patients with osteoporosis. See the ICSI Technology Assessment Report #53, [Biochemical Markers for Bone Turnover in Osteoporosis](#), for more information.

Certain diseases are commonly associated with bone loss. These diseases are listed in Annotation Appendix A, "Secondary Causes of Osteoporosis," in the original guideline document. In broad categories, these include chronic inflammatory autoimmune conditions, endocrinopathies, malignancies, and malabsorptive states.

Evidence supporting this recommendation is of classes: D, R

#### 15. Address Options for Prevention and Treatment of Osteoporosis

Please see the medication tables in Annotation Appendix B of the original guideline document, "Recommended Pharmacologic Agents" and Discussion #15 for specific information on pharmacologic agents for treatment and prevention of osteoporosis.

In addition to pharmacological agents for osteoporosis all patients should supplement their dietary intake of calcium and vitamin D if it is not adequate (see Annotation #5 "Discuss Primary Prevention of Fractures"). Physical therapy may also be considered.

### Osteoporosis Prevention

Estrogen has traditionally been considered first-line therapy for prevention of osteoporosis in postmenopausal women, but if the only reason estrogen therapy has been prescribed is for osteoporosis prevention, other therapies should be considered. If the decision is made to discontinue estrogen, a BMD should be obtained to determine if other bone loss prevention therapies are needed. Other medications for prevention include bisphosphonates and raloxifene.

### Osteoporosis Treatment

Bisphosphonates have the strongest data showing risk reductions in both vertebral, hip, and other nonvertebral fractures. Other treatments include raloxifene and calcitonin.

Excellent clinical trial data supports the use of oral bisphosphonates for preventing fractures in patients diagnosed with postmenopausal osteopenia or osteoporosis (with previous vertebral fractures). The best clinical trials have been done with alendronate (Fosamax®) and risedronate (Actonel®). [Conclusion Grade I: See Conclusion Grading Worksheet - Appendix B of the original guideline document, - Annotation #15 (Bisphosphonates for Primary Osteoporosis)].

Good clinical trial data support the use of alendronate for preventing bone loss in men diagnosed with osteoporosis. [Conclusion Grade I: See Conclusion Grading Worksheet - Appendix B of the original guideline document, - Annotation #15 (Bisphosphonates for Primary Osteoporosis)].

Clinical trial data supports the use of oral bisphosphonates for reducing bone loss in men and women diagnosed with glucocorticoid-induced bone loss. The best clinical trials have been done with alendronate (Fosamax®) and risedronate (Actonel®). [Conclusion Grade II: See Conclusion Grading Worksheet - Appendix C in the original guideline document, - Annotation # 15 (Bisphosphonates for Glucocorticoid-induced Bone Loss)].

Clinical trial data suggests that oral bisphosphonates may reduce fracture risk in men and women diagnosed with glucocorticoid-induced bone loss. [Conclusion Grade III: See Conclusion Grading Worksheet - Appendix C of the original guideline, - Annotation #15 (Bisphosphonates for Glucocorticoid-induced Bone Loss)].

## Post-transplantation Bone Loss

Antiresorptive therapy may be effective at preventing bone density loss after transplantation. Considering the rates of bone loss after transplantation described in Annotation #3, bone mineral density testing should be performed every 6 months until bone mineral density is shown to be stable or improving on therapies for osteoporosis. Studies demonstrate that standard calcium and vitamin D supplementation, with or without calcitonin, is not able to prevent bone loss after transplantation. Other studies indicate that pharmacologic vitamin D preparations or intravenous pamidronate or oral alendronate are more likely to prevent bone loss after transplantation.

## Alternative and Complementary Agents for Prevention and Treatment of Osteoporosis

There is preliminary data on a number of non-Food and Drug Administration (FDA) approved substances for possible use in prevention and treatment of osteoporosis. These include phytoestrogens, synthetic isoflavones such as ipriflavone, natural progesterone cream, magnesium, vitamin K and eicosapentaenoic acid. There is very limited data from randomized controlled trials of these agents for prevention or treatment of osteoporosis. A recently reported, multicenter randomized trial of ipriflavone showed no significant effect on bone density or risk of vertebral fractures.

Evidence supporting this recommendation is of classes: A, B, C, D, M, R

## 16. Follow-Up Testing After Pharmacologic Intervention

Sequential bone density testing may be used to monitor antiresorptive therapy. The key factor is understanding that this tool is limited by the calculated precision of the machine and operator at a particular body site. It is imperative that a central site (lumbar spine and/or total hip) be used for follow-up testing to provide information about a change in BMD. There is not adequate data to recommend using any peripheral site for follow-up bone density testing, including forearm dual x-ray absorptiometry (DXA), calcaneal DXA, or calcaneal ultrasound. The best follow-up evaluation will be done on the same or similar bone density machine by the same trained bone density technologist.

Despite its limitations, bone density testing with DXA, with coefficients of variation in the range of 1 to 2%, remains one of the most precise measurements used in medical practice. Controversy exists as to whether follow-up testing is necessary in all patients, but if it is performed, it should be done after one to two years of therapy. In patients at particularly high risk for accelerated bone loss, such as the glucocorticoid-treated patient or a woman in early menopause who is not using estrogen replacement, follow-up bone density testing may be indicated annually.

Evidence supporting this recommendation is of classes: A, C, D, M, R

## Definitions:

### Conclusion Grades:

Grade I: The evidence consists of results from studies of strong design for answering the question addressed. The results are both clinically important and consistent with minor exceptions at most. The results are free of any significant doubts about generalizability, bias, and flaws in research design. Studies with negative results have sufficiently large samples to have adequate statistical power.

Grade II: The evidence consists of results from studies of strong design for answering the question addressed, but there is some uncertainty attached to the conclusion because of inconsistencies among the results from the studies or because of minor doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from weaker designs for the question addressed, but the results have been confirmed in separate studies and are consistent with minor exceptions at most.

Grade III: The evidence consists of results from studies of strong design for answering the question addressed, but there is substantial uncertainty attached to the conclusion because of inconsistencies among the results of different studies or because of serious doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from a limited number of studies of weak design for answering the question addressed.

Grade Not Assignable: There is no evidence available that directly supports or refutes the conclusion.

### Classes of Research Reports:

#### A. Primary Reports of New Data Collection:

##### Class A:

- Randomized, controlled trial

##### Class B:

- Cohort study

##### Class C:

- Non-randomized trial with concurrent or historical controls
- Case-control study
- Study of sensitivity and specificity of a diagnostic test
- Population-based descriptive study

##### Class D:

- Cross-sectional study
- Case series
- Case report

B. Reports that Synthesize or Reflect upon Collections of Primary Reports:

Class M:

- Meta-analysis
- Systematic review
- Decision analysis
- Cost-effectiveness analysis

Class R:

- Consensus statement
- Consensus report
- Narrative review

Class X:

- Medical opinion

CLINICAL ALGORITHM(S)

A detailed and annotated clinical algorithm is provided for [Bone Health](#).

## EVIDENCE SUPPORTING THE RECOMMENDATIONS

### TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The guideline contains an annotated bibliography and discussion of the evidence supporting each recommendation. The type of supporting evidence is classified for selected recommendations (see "Major Recommendations").

In addition, key conclusions contained in the Work Group's algorithm are supported by a grading worksheet that summarizes the important studies pertaining to the conclusion. The type and quality of the evidence supporting these key recommendations (i.e., choice among alternative therapeutic approaches) is graded for each study.

## BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

### POTENTIAL BENEFITS

#### Overall Benefits

- Appropriate recognition, prevention and treatment of osteoporosis and subsequent decrease in bone loss and fracture risk and increase in bone health

- Improved diagnostic and therapeutic follow-up of adults presenting with a history of low-impact fracture
- Increased evaluation for osteoporosis risk factors in all adults presenting for a preventive visit
- Increased follow-up testing of patients on long term hormone replacement therapy (HRT)

### Specific Benefits

- Calcium. Comprehensive review of the relationship of calcium intake and bone health reported that calcium slows age-related bone loss and may reduce osteoporotic fracture risk. Both dairy sources and calcium supplements are related to promoting bone health. Calcium enhances therapy with antiresorptive medication, such as estrogen.
- Vitamin D. Studies of combined calcium and vitamin D supplementation have demonstrated reductions in bone loss and fractures.
- Measures to prevent falls. Preventing falls reduces fractures. Modifying environmental and personal risk factors can be effective in reducing falls. Home visits have been shown to help with this. Also, soft hip protector pads have been shown to reduce hip fractures in frail, elderly adults in community-based health care centers.
- Bone density measurement. Measurements of bone mineral density (BMD) can predict fracture risk, and allow for the identification of people who are at increased risk of fracture. Reviews of prospective cohort studies and case control studies have documented a direct relationship between decreasing bone mineral density and increasing bone fracture risk. Additionally, there is strong evidence that increases in bone mineral density with therapy for osteoporosis lead to substantial reduction in fracture incidence.
- Estrogen. The use of supplemental estrogen in the immediate postmenopause has been well accepted in preventing the rapid loss of bone that occurs in this interval. Supplemental estrogen not only retards accelerated bone loss, but has also been shown to create a gain in bone density.
- Bisphosphonates. Excellent clinical trial data supports the use of oral bisphosphonates for preventing fractures in patients diagnosed with postmenopausal osteopenia or osteoporosis. The best clinical trials have been done with alendronate (Fosamax®) and risedronate (Actonel®). Clinical trial data suggest that oral bisphosphonates may reduce fracture risk in men and women diagnosed with glucocorticoid-induced bone loss.
- Calcitonin. For treatment of osteoporosis in postmenopausal women, calcitonin has shown a 33% risk reduction in vertebral fractures with calcitonin 200 IU daily compared with placebo (RR 0.67, 95% CI 0.47-0.97, p = 0.03).

### Subgroups Most Likely to Benefit

Women with prior fracture and low bone density are the most responsive to antiresorptive therapy. The largest therapy induced bone mineral density (BMD) increase is observed in patients with the lowest bone mineral density and vertebral fractures, the population at highest risk.

### POTENTIAL HARMS

## Side Effects of Medication

- Raloxifene. Worsening hot flashes and leg cramps, and increased risk of thromboembolic events are reported side effects of raloxifene.
- Bisphosphonates. Oral bisphosphonate preparations have the potential to cause upper gastrointestinal erosions and ulcerations on rare occasions.
- Calcitonin. Nausea, flushing, rhinitis with nasal spray
- Estrogen. Bloating, breast tenderness, uterine bleeding, increased risk of thromboembolic events

See Appendix B of the original guideline document for a more complete list of adverse drug reactions.

## CONTRAINDICATIONS

### CONTRAINDICATIONS

- Alendronate (Fosamax). Contraindications include abnormalities of the esophagus which delay esophageal emptying, inability to stand or sit upright for at least 30 minutes, hypersensitivity, and hypocalcemia. It is not recommended for patients with creatinine clearance (CrCL) equal or less than 35 ml/min.
- Risedronate (Actonel). Contraindications include inability to stand or sit upright for at least 30 minutes, hypersensitivity, and hypocalcemia. It is not recommended for patients with CrCl equal or less than 30 ml/min.
- Raloxifene (Evista). Contraindications include pregnancy, history of thromboembolism, and hypersensitivity.
- Teriparatide (Forteo). Contraindications include Paget's disease, children, prior radiation therapy involving the skeleton, bone metastases or history of skeletal malignancies, metabolic bone disease (other than osteoporosis), hypercalcemia, and pregnant and nursing women.
- Calcitonin-salmon (Miacalcin nasal spray). Contraindications include hypersensitivity.
- Estrogens. Contraindications include pregnancy, history of thromboembolic disorders, breast cancer, estrogen dependent neoplasia, undiagnosed abnormal vaginal bleeding, and hypersensitivity.

## QUALIFYING STATEMENTS

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- These clinical guidelines are designed to assist clinicians by providing an analytical framework for the evaluation and treatment of patients, and are not intended either to replace a clinician's judgment or to establish a protocol for all patients with a particular condition. A guideline will rarely establish the only approach to a problem.
- This medical guideline should not be construed as medical advice or medical opinion related to any specific facts or circumstances. Patients are urged to consult a health care professional regarding their own situation and any specific medical questions they may have.

- There is very limited data from randomized controlled trials of alternative and complementary agents for prevention or treatment of osteoporosis.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

Once a guideline is approved for general implementation, a medical group can choose to concentrate on the implementation of that guideline. When four or more groups choose the same guideline to implement and they wish to collaborate with others, they may form an action group.

In the action group, each medical group sets specific goals they plan to achieve in improving patient care based on the particular guideline(s). Each medical group shares its experiences and supporting measurement results within the action group. This sharing facilitates a collaborative learning environment. Action group learnings are also documented and shared with interested medical groups within the collaborative.

Currently, action groups may focus on one guideline or a set of guidelines such as hypertension, lipid treatment, and tobacco cessation.

The following detailed measurement strategies are presented to help close the gap between clinical practice and the guideline recommendations.

#### Priority Aims and Suggested Measures of Health Care Systems

1. Improve diagnostic and therapeutic follow-up of adults presenting with a history of low-impact fracture.

Possible measures of accomplishing this aim:

- a. Percentage of adults presenting with a history of low-impact fracture who have had bone densitometry
  - b. Percentage of postmenopausal women and men with a history of low-impact fracture identified as having low bone mass offered treatment for osteoporosis
  - c. Percentage of adults with a history of low-impact fracture offered treatment for osteoporosis
  - d. Percentage of adults with a history of low-impact fracture with documentation of discussion with a health care provider of osteoporosis risk
2. Increase the evaluation for osteoporosis risk factors in all adults presenting for a preventive visit.

Possible measures for accomplishing this aim:

- a. Percentage of patients presenting for a preventive visit with documentation of assessment of risk factors for osteoporosis
- b. Percentage of patients at risk for fracture who have had bone densitometry

3. Increase follow-up testing of patients on long term hormone replacement therapy (HRT).

Possible measure for accomplishing this aim:

- a. Percentage of patients on long term HRT who have had follow-up bone densitometry.

Note: At this point in development for this guideline, there are no specifications written for possible measures listed above. Institute for Clinical Systems Improvement (ICSI) will seek input from the medical groups on what measures are of most use as they implement the guideline. In a future revision of the guideline, one or two measurement specifications may be included.

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Living with Illness  
Staying Healthy

### IOM DOMAIN

Effectiveness  
Patient-centeredness

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

Institute for Clinical Systems Improvement (ICSI). Diagnosis and treatment of osteoporosis. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2004 Jul. 66 p. [175 references]

### ADAPTATION

Not applicable: The guideline was not adapted from another source.

### DATE RELEASED

2002 Aug (revised 2004 Jul)

### GUIDELINE DEVELOPER(S)

Institute for Clinical Systems Improvement - Private Nonprofit Organization

### GUIDELINE DEVELOPER COMMENT

Organizations participating in the Institute for Clinical Systems Improvement (ICSI): Affiliated Community Medical Centers, Allina Medical Clinic, Altru Health

System, Aspen Medical Group, Avera Health, CentraCare, Columbia Park Medical Group, Community-University Health Care Center, Dakota Clinic, ENT SpecialtyCare, Fairview Health Services, Family HealthServices Minnesota, Family Practice Medical Center, Gateway Family Health Clinic, Gillette Children's Specialty Healthcare, Grand Itasca Clinic and Hospital, Hamm Clinic, HealthEast Care System, HealthPartners Central Minnesota Clinics, HealthPartners Medical Group and Clinics, Hennepin Faculty Associates, Hutchinson Area Health Care, Hutchinson Medical Center, Lakeview Clinic, Mayo Clinic, Mercy Hospital and Health Care Center, MeritCare, Minnesota Gastroenterology, Montevideo Clinic, North Clinic, North Memorial Health Care, North Suburban Family Physicians, NorthPoint Health & Wellness Center, Northwest Family Physicians, Olmsted Medical Center, Park Nicollet Health Services, Quello Clinic, Ridgeview Medical Center, River Falls Medical Clinic, St. Mary's/Duluth Clinic Health System, St. Paul Heart Clinic, Sioux Valley Hospitals and Health System, Southside Community Health Services, Stillwater Medical Group, SuperiorHealth Medical Group, University of Minnesota Physicians, Winona Clinic, Winona Health

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## SOURCE(S) OF FUNDING

The following Minnesota health plans provide direct financial support: Blue Cross and Blue Shield of Minnesota, HealthPartners, Medica, Metropolitan Health Plan, PreferredOne, and UCare Minnesota. In-kind support is provided by the Institute for Clinical Systems Improvement's (ICSI) members.

## GUIDELINE COMMITTEE

Committee on Evidence-Based Practice

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## FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

In the interest of full disclosure, Institute for Clinical Systems Improvement (ICSI) has adopted a policy of revealing relationships work group members have with companies that sell products or services that are relevant to this guideline topic.

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John Schousboe, MD receives grant support from Merck, Procter & Gamble, and Novartis, is a consultant to Procter & Gamble, and is a member of the Speaker's Bureau for Eli Lilly.

Christine Simonelli, MD receives grant support from Merck, Novartis, Eli Lilly, and Procter & Gamble, serves as a consultant for Procter & Gamble and Merck, and is a member of the Speaker's Bureau for Merck, Eli Lilly, and Procter & Gamble.

Bart Clarke, MD, receives grant support and serves as a consultant for Merck.

Renee Compo, RN, CNP, is a member of the speaker's bureau for Wyeth.

No other work group members have potential conflicts of interest to disclose.

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#### GUIDELINE STATUS

This is the current release of the guideline.

It updates a previous version: Institute for Clinical Systems Improvement (ICSI). Diagnosis and treatment of osteoporosis. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2003 Jul. 68 p.

#### GUIDELINE AVAILABILITY

Electronic copies: Available from the [Institute for Clinical Systems Improvement \(ICSI\) Web site](http://www.icsi.org).

Print copies: Available from ICSI, 8009 34th Avenue South, Suite 1200, Bloomington, MN 55425; telephone, (952) 814-7060; fax, (952) 858-9675; Web site: [www.icsi.org](http://www.icsi.org); e-mail: [icsi.info@icsi.org](mailto:icsi.info@icsi.org).

#### AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Diagnosis and treatment of osteoporosis. In: ICSI pocket guidelines. April 2003 edition. Bloomington (MN): Institute for Clinical Systems Improvement, 2003 Mar. p. 308-10.

Print copies: Available from ICSI, 8009 34th Avenue South, Suite 1200, Bloomington, MN 55425; telephone, (952) 814-7060; fax, (952) 858-9675; Web site: [www.icsi.org](http://www.icsi.org); e-mail: [icsi.info@icsi.org](mailto:icsi.info@icsi.org).

## PATIENT RESOURCES

None available

## NGC STATUS

This summary was completed by ECRI on December 24, 2002. The information was verified by the guideline developer on January 23, 2003. This summary was updated by ECRI on April 12, 2004 and on September 16, 2004.

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Date Modified: 11/15/2004

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